REMARKS

With entry of this Amendment claims 37-40, 54 and 59-82 are pending in the application. Claims 1-36, 41-53, and 55-58 were previously cancelled without prejudice to their elective further prosecution in any related application(s). By this Amendment, claims 37 and 54 have been amended for clarity and without prejudice to correct formalities or more distinctly recite certain aspects of the invention. All of the amendments herein are fully supported by the specification, and no new matter has been added to the application. Entry of this Amendment and consideration of the accompanying remarks is respectfully requested.

Patentability Under 35 USC § 112, First Paragraph

Claims 37-40, 54, 59-65 and 68-82 continue to be rejected under 35 USC § 112, first paragraph for alleged failure to comply with the written description requirement (Office Action, pages 2-3).

Applicants respectfully traverse the foregoing grounds of rejection set forth at pp. 2-3 of the Office Action, and submit that the disclosure fully describes and enables the subject matter of claims 37-40, 54 and 59-65 and 68-82

The Office essentially offers two grounds for making this rejection. First, the Office suggests that the claims should contain a requirement that the MHC class II construct must be specific for the antigenic determinant which is linked to the MHC class II construct. However, this position is inconsistent with the experimental results set forth in the application. For example, the specification at page 55, lines 23-28 summarizes an experiment performed using the same MHC Class II $\beta 1\alpha 1$ construct containing either the MBP-69-89 peptide antigen or the CM-2 peptide antigen. The experiment shows that the different bound epitopes were capable of directing the same MHC Class II $\beta 1\alpha 1$ construct in an antigen specific manner. In particular, the specification indicates the following:

> Direct binding studies using the A1 hybridoma specific for MBP-72-89 showed distinct staining with $\beta 1\alpha 1$/MBP-69-89, with a ten-fold increase in MF1 over background, and was not stained with $\beta 1\alpha 1$/CM-2 nor "empty" $\beta 1\alpha 1$. In a reciprocal manner, binding studies using a CM-2 specific cell line showed strong staining with $\beta 1\alpha 1$/CM-2 and no staining with $\beta 1\alpha 1$/MBP-69-89. Thus, bound epitope directed specific interaction of the $\beta 1\alpha 1$/peptide complexes. [Specification, page 55, lines 23-28]

Similarly, Example 12 describes an experiment performed using the same MHC Class II $\beta 1\alpha 1$ construct containing either covalently bound MBP85-99 peptide (RTL303) or CABL peptide (RTL311). This experiment also shows that the different bound peptides could utilize the same MHC Class II $\beta 1\alpha 1$ construct in an antigen specific manner. In particular, with respect to IL-10 production, the specification indicates the following:

> [U]pon treatment with RTL303, clone MR#3-1...dramatically increased its production of IL-10 (Fig. 24A). IL-10 appeared within 24 hours after addition of RTL303 and its production continued for more than 72 hours, to three orders of magnitude above the untreated or RTL311 treated control....Similarly, after treatment with RTL311, Clone MR#27-87 (CABL specific) also showed a dramatic increase in production of IL-10 within 24 hours that continued for greater than 72 hours above the untreated or RTL303 treated control (Fig. 24B)....*The switch to IL-10 production was exquisitely Ag-specific, with the clones responding only to the cognate RTL carrying peptide antigen for which the clones were specific.* [Specification, page 81, lines 9-21, *emphasis added*]

Clearly, the subject invention does not require that the MHC Class II construct be specific to the antigenic determinant which is linked to the MHC Class II construct, although this is not precluded by the claims. All that is required is that the MHC Class II polypeptide be non-covalently associated or covalently conjugated with the antigenic determinant and that the immune response in the subject against the antigenic determinant be reduced by the MHC Class II polypeptide non-covalently associated or covalently conjugated with the antigenic determinant. All independent claims have been previously amended to recite these requirements.

Second, the Office indicates that "[t]he breadth of Applicant's claim is such that it recites a composition for the treatment of unrelated autoimmune diseases with a fragment of the MHC Class II extracellular domain, as there is no requirement to match the MHC class II molecule to either the determinant or disease." [Office Action, page 3] With respect to this issue, as discussed in great detail above, it is not necessary that the MHC Class II $\beta 1\alpha 1$ construct be "matched" to the antigenic determinant, that is, the MHC class II construct need not be specific for the antigenic determinant which is linked to the MHC class II construct. Furthermore, it should be noted that the claims already require that the immune response being treated be antigen-specific. In particular, independent claim 37 is directed to the reduction of "an immune response against an antigenic determinant" while independent claim 54 is directed to "treating a disease caused by antigen-specific T-cells." Such methodology, since the immune response

being modified is "antigen-specific," and is directed "against the antigenic determinant", it is axiomatic that the antigenic determinant is "matched" with the targeted disease (i.e., that the determinant is a specific target of the immune response associated with the targeted disease). In this context, for the purpose of clarity and to more distinctly recite certain aspects of the invention, claim 37 has been amended to recite, like claim 54, that the immune response is "antigen-specific."

Finally, in view of the foregoing, it is clear that since claim 54 is allowable, Claims 66 and 67 are also allowable and need not be rewritten in independent form, as suggested by the Office.

Applicants have disclosed and enabled the use of MHC Class II $\beta 1\alpha 1$ constructs with different antigenic determinants in order to reduce an immune response in an antigen-specific manner. One of ordinary skill in the art, upon reading the specification, would understand that such constructs, being applicable to different antigenic determinants, could be generally applied to reduce the immune response caused by various immune disorders. Indeed, as noted by Applicants "[b]ecause of its simplicity, biological properties, and structural similarity with human class II homologs, the $\beta 1\alpha 1$ construct represents a template for producing a novel class of TCR ligands." [Specification, page 55, lines 20-22] As such, Applicants are entitled to claim the full scope of their invention.

CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this application are in condition for allowance, and an official action to that end is urged. If the Examiner believes that a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at (206) 381-3300.

Date: January 11, 2006

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